



CME/CE Clinical Précis
for the Interprofessional Health Care Team

Hip Fractures: Which Interventions Are Effective For Managing Pain?

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Hip Fractures: Which Interventions Are Effective For Managing Pain?

Learning Objectives

Based on the findings from AHRQ's comparative effectiveness review on management strategies for women with noncyclic chronic pelvic pain:

1. Compare the efficacy and safety of interventions for controlling acute and chronic pain related to hip fractures
2. Summarize the effectiveness of pain interventions on mortality, functional status, health-related quality of life, and health services utilization
3. Determine the safety and efficacy of pain interventions among specific patient subpopulations
4. Apply the systematic review findings to educate patients about treatment options for pain management following hip fractures

Background and Public Health Burden of Hip Fractures

Hip fractures are a significant public health issue, leading to substantial rates of morbidity and mortality. The incidence of hip fractures ranges from 22.5 and 23.9 per 100,000 men and women, respectively. By age 80, these ranges increase to 630.2 and 1,289.³ for men and women, respectively.¹⁻⁴ With short-term mortality rates ranging from 25 percent for women to 37 percent for men during the first year following the fracture, the health impact can be devastating. Approximately 25 percent to 50 percent of older adults with hip fractures do not return to their pre-fracture level of function until 6 months after the injury occurred. This poor functional recovery contributes to a

high utilization of health resources and increasing health care costs.

Hip fractures are also associated with severe pain, which can lead to delirium, depression, sleep disturbance, and decreased response to interventions for other comorbidities.⁵⁻⁷ As a result, the consequences of poorly managed postoperative pain can further complicate treatment and recovery. Acute treatment of pain is necessary, since poor management is associated with delayed ambulation, pulmonary complications, and delays in patient transitions to different levels of care.⁸

Interventions intended to alleviate pain are divided according to the timing of the operation and include: pre-, peri-, and postoperative. Preoperative

interventions traditionally use systemic analgesia. Nerve blocks, which incorporate the use of analgesics to block nerve impulses from reaching the sensory cortex, have recently been introduced as a mechanism to alleviate pain. Intraoperative interventions typically incorporate general anesthesia and systemic analgesia. Neuraxial anesthesia has been commonly used as a substitute for general anesthesia. Postoperative pain management entails the use of a multitude of interventions including systemic analgesia, nerve blocks, physical therapy, and transcutaneous electrical nerve stimulation (TENS). Combined approaches that are used to disrupt pain by different mechanisms are known as “multimodal” pain management.

AHRQ’s Comparative Effectiveness Review

In an effort to synthesize information from studies comparing the efficacy of interventions used to treat pain associated with hip fractures, the Agency for Healthcare Research and Quality (AHRQ) commissioned a comparative effectiveness review which was published in May 2011.⁹ A preliminary review was conducted by the University of Alberta Evidence-based Practice Center (UAEPC) in order to determine the quantity of available evidence and to draft key questions for the comparative effectiveness review (CER). AHRQ and the Scientific Resource Center invited a technical expert panel (TEP) to provide input in the development of key questions for the report. After public commentary, the finalized key questions were sent to AHRQ for approval. The clinical study literature was summarized and reviewed using the PICOTS (population, intervention, comparison, outcome, timing, and setting) framework. Evidence identified from these outcomes was examined in detail to determine the strength

of evidence of the studies. The key questions were developed according to the criteria listed below:

- **P**opulation: Elderly patients experiencing pain due to non-pathological, low-impact injury hip fractures
- **I**nterventions: Pain management methods, including systemic analgesia, neuraxial anesthesia, nerve blocks, traction, TENS, rehabilitation, complementary and alternative methods, and multimodal approaches
- **C**omparators: usual care (nonopioid and opioid systemic analgesia) and/or other interventions
- **O**utcomes: pain intensity, mental status, 30-day mortality, and serious adverse events (stroke, myocardial infarction, renal failure)
- **T**iming: acute care, within 30 days of fracture

- **S**etting: acute care

Process for Conducting the Review

Topics for the review were nominated through an open public process, which included submissions from professional

organizations, policymakers, health care professionals, and the private sector. Investigators at the UAEPC in Edmonton, Alberta, Canada researched databases including MEDLINE, Cochrane Central Register of Controlled Trials, and Cumulative Index to Nursing and Allied Health Literature, including studies published from 1990 to 2010. The reviewers also searched medical journals, relevant reviews, and literature from scientific meetings and public clinical trial registries. The quality of the studies was evaluated by 2 independent reviewers with criteria including the extent of treatment blinding, description of the randomization procedure, adequate control of potential confounders or bias, appropriate methods for addressing incomplete outcome data, and whether funding sources and conflicts of interest were identified. Findings from the literature search are illustrated in Table 1.

The strength of evidence was classified into 4 main categories which are detailed in *AHRQ’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.¹⁰ To evaluate the evidence, the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) working group developed an instrument that

Table 1. Pain Management Interventions for Hip Fracture Included in the AHRQ Review

Intervention	Studies (N)	Timing
Systemic analgesia	3	Pre- and postoperative
Anesthesia	30	Intraoperative
Nerve Blocks	32	Pre-, intra-, and postoperative
Traction	11	Preoperative
TENS	2	Pre- and postoperative
CAM interventions	2	Preoperative
Rehabilitation	1	Postoperative
Multimodal management	2	Pre- and postoperative

Source: Derived from Abou-Setta AM, Beaupre LA, Jones CA, et al. Pain Management Interventions for Hip Fracture. Comparative Effectiveness Review No. 30. Rockville, MD. Agency for Healthcare Research and Quality. May 2011. Available at: http://www.effectivehealthcare.ahrq.gov/ehc/products/95/678/CER30_FinalReview_20110517.pdf.

considers factors such as directness, precision, consistency across studies of the same and different designs, magnitude of effect, applicability, and the potential for publication bias. The evidence was graded as *high*, *moderate*, *low*, or *insufficient*. The first 3 of these grades indicate the investigators' confidence in the extent to which the evidence reflects true, or systematic, treatment effects. A grade of *insufficient* indicates that evidence does not either exist or permit the estimation of effects.

Summary of Key Questions

The UAEPCC investigators based their comparative effectiveness review on 4 main questions. The key questions, which are summarized below, compared usual (standard care) with other pain management interventions for older adults (≥ 50 years) admitted to the hospital following a hip fracture.

QUESTION 1

- What are the comparative effects of various pharmacological and nonpharmacological pain management interventions on acute and chronic pain?

This question focuses on the primary outcomes of interest.

QUESTION 2

- What are the comparative effects of various pharmacological and nonpharmacological pain management interventions on secondary outcomes?

Secondary outcomes of interest included 30-day mortality, length of hospitalization, delirium associated with pain, additional pain medication use, quality of sleep, and health-related quality of life.

QUESTION 3

- What are the comparative adverse effects associated with different pain management interventions?

Adverse events included gastrointestinal disturbance, headaches, infection, allergic reaction, bradycardia, nausea or vomiting, neurologic complications, myocardial infarction, stroke, sensory deficits or motor weakness, pulmonary embolism, and deep venous thrombosis.

QUESTION 4

- How do the effectiveness and safety of pain management interventions vary in different subpopulations?

Pain Management Interventions Overview

Interventions targeting the pain associated with hip fractures can be divided into pharmacological and nonpharmacological treatment therapies. Systemic analgesia, medications used in nerve blocks, and neuraxial anesthesia are examples of pharmacological interventions. TENS, acupressure, and fracture stabilization via traction are nonpharmacologic pain interventions.

The choice of pain management interventions are guided by prior medical status of the patient, fracture characteristics, and requirements of the treatment plan. Comorbidities can also affect the perception of pain and response to pain treatment. Usual care for pain following a hip fracture includes systemic analgesia, primarily using nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids. However, complications associated with opioid use can include altered mental status changes, nausea and vomiting, respiratory depression, and constipation. Similarly, NSAID side effects of gastrointestinal bleeding and renal toxicity are particularly problematic

in older adults. Accordingly, AHRQ sought to determine which alternative methods could be effective and safe for pain management in older adults with hip fracture.

Comparative Effectiveness of Interventions for Acute Pain Relief

With a total of 83 studies included in the review, consisting of 64 randomized controlled trials (RCTs), 5 nonrandomized controlled trials (nRCTs), and 14 cohort studies, the participants were predominantly females older than 75 years of age without cognitive impairment. The cohort studies were generally of moderate quality, while many trials were low quality with a high or unclear risk of bias. Peri- and postoperative management of pain and reported mortality and adverse events associated with the interventions were evaluated. There were no studies that addressed long-term pain, and other outcomes including bradycardia, neurologic complications, myocardial infarction, stroke, sensory deficits or motor weakness, pulmonary embolism, and deep venous thrombosis were rarely reported.

Overall, nerve blocks were proven to be effective at relieving acute pain. Most studies did not indicate whether or not nerve blocks affected rehabilitation, including ambulation or mobility, if sensory or motor effects were present. Potential reductions in acute pain were found for acupressure, relaxation therapy, and TENS; however, further evidence is needed to fully determine the effects of these interventions. Postoperative physical therapy showed some evidence for improvements in pain status, but the quality of the evidence was insufficient. Parecoxib, a systemic analgesic not available for use in North America, showed some potential as a possible alternative

to NSAIDs and intramuscular opioid injections. Preoperative traction and spinal anesthesia were not consistently effective at improving pain status when compared with standard care.

**Take-Home Messages:
Comparative Effectiveness
of Pain Management
Interventions for Hip
Fractures in Older Adults**

Nerve Blocks:

- Reduce the intensity of acute pain (3-in-1, fascia iliaca, femoral, psoas compartment, and combined obturator and femoral blocks) ■■
- Decrease the incidence of delirium ■■
- Are equally effective compared to spinal anesthesia for acute pain relief (psoas compartment, posterior lumbar plexus, and combined lumbar and sacral plexus blocks) ■

Skin Traction:

- Does not reduce the intensity of acute pain ■

Rehabilitation, Acupressure, Relaxation Therapy, TENS:

- Evidence for pain relief was insufficient to reach firm conclusions for pain relief

■■ = Medium strength of evidence
■ = Low strength of evidence

Measuring Pain Levels

Self-reported pain is the “gold standard” for measuring the character and intensity of pain.⁵ The presence of dementia or delirium – found in a large proportion of patients with hip fracture - may interfere considerably

with a patient’s ability to self-report pain and complicates pain assessment and management.¹¹⁻¹⁴

The Visual Analogue Scale (VAS), the most commonly used instrument to measure pain levels in research studies, consists of a 100 mm unmarked line with “no pain” on the far left and “worst pain ever” on the far right. Respondents point to or mark a line on the scale that indicates how much pain they are feeling. Whereas results of the the VAS are highly reliable, valid, and allow scaling of the magnitude of pain intensity, they are relatively difficult for patients to understand – particularly in the setting of mild cognitive impairment – and are not widely used in routine clinical practice.

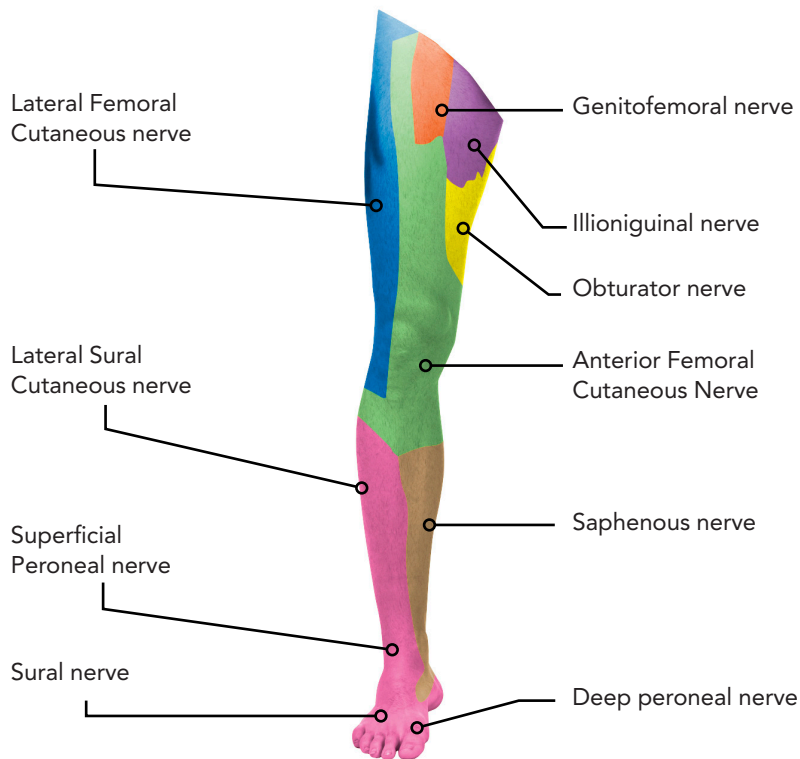
Other more common tools used to measure pain in the clinical setting include numeric rating scales, verbal descriptive scales, and pictorial or cartoon scales. Numeric scales, which

generally have numbers between 0 and 10, are used to rate how much pain the patient is currently feeling, with higher numbers indicating a greater pain intensity. The widely accepted range for clinically significant absolute pain reduction is 20 percent to 30 percent (2-3 points on a ten point scale), which corresponds approximately to a 30 mm of absolute difference on the VAS.

Nerve Blocks for Acute Pain

There are various types of nerve blockades used to manage pain for the hip fracture patient including the femoral, 3-in-1 (femoral, obturator, and sciatic nerves), fascia iliaca, psoas (lumbar plexus), and continuous epidural. The nerves targeted in the different nerve block interventions are depicted in Figure 1. Local anesthetics such as bupivacaine are used in regional nerve blocks to prevent the conduction of pain signals to the central nervous system (CNS). Clonidine, morphine,

Figure 1: Nerves Targeted for Nerve Blockade Intervention



Used with permission from www.nysora.com.

fentanyl, and sufentanil are additional medications commonly used in nerve blocks.

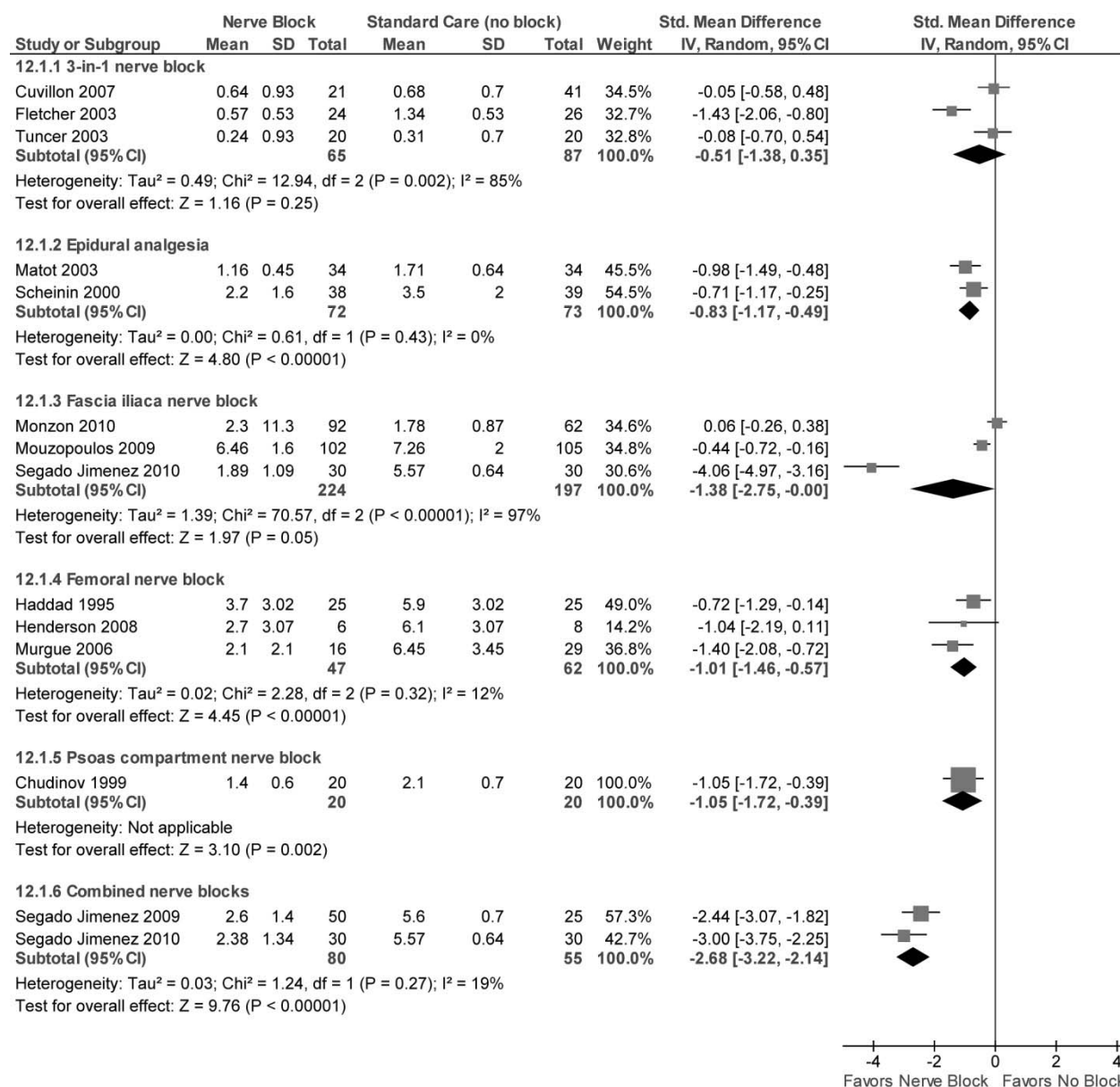
Post-treatment acute pain was reported in 13 RCTs¹⁵⁻²⁷ which are depicted in Figure 2. In 1 RCT,²⁸ a statistically significant difference in the frequency of postoperative pain on the first day was found in favor of nerve blocks compared with no nerve block (7/25 vs 20/25; odds ratio [OR]=0.10; 95 percent confidence

interval [CI] = 0.03 to 0.36; $P=.0005$). Four trials reported pain on movement,^{18-20,27} but the heterogeneity among the studies prevented the completion of a meta-analysis of pooled results from the studies. Pooled results from 2 RCTs^{20,26} found significant reductions in pain favoring the 3-in-1 nerve block over no block (standardize mean difference [SMD] = -1.02; 95 percent CI = -1.83 to -0.21; $P=.01$). Another RCT²⁰, which had a high risk for bias, found significant

improvements in pain relief on the 10 cm VAS favoring nerve blocks using preoperative epidural analgesia over no nerve block (MD=-2.30; 95 percent CI = -2.92 to -1.68; $P<.00001$). Results from 1 RCT²⁹ found no significant differences in pain relief for femoral nerve blocks compared with no nerve block when using the 5-point Verbal Rating Scale.

Three RCTs,^{19,26,29} with a moderate strength of evidence, reported post-

Figure 2. Systemic Analgesics and Anesthesia Interventions and Mechanisms of Action



Derived from Abou-Setta AM, Beaupre LA, Jones CA, et al. Pain Management Interventions for Hip Fracture. Comparative Effectiveness Review No. 30. Rockville, MD. Agency for Healthcare Research and Quality. May 2011. Available at: http://www.effectivehealthcare.ahrq.gov/ehc/products/95/678/CER30_FinalReview_20110517.pdf.

treatment pain on rest for nerve block interventions. Compared with standard care, postoperative 3-in-1 nerve blocks did not lead to significant differences in pain relief on the 10 cm VAS.²⁶ However, another RCT¹⁹ with a high risk for bias found a statistically significant difference in pain relief favoring nerve blocks over standard care according to the 10 cm VAS (MD = -0.55; 95 percent CI = -0.81 to -0.29; $P<.0001$). Similarly, femoral nerve blocks were significantly favored over standard care for relief of pain on rest using the 5-point Verbal Rating Scale (MD = 0.18; 95 percent CI = 0.03 to 0.33) $P=.02$). In 3 RCTs evaluating nerve block compared with neuraxial anesthesia,^{26,30,31} no statistically significant differences were found for acute pain relief between the 2 groups (MD = -0.35; 95 percent CI = -1.10 to 0.39; $P=.35$).

According to studies included in the AHRQ review, most nerve blocks were able to reduce the intensity of acute pain and the incidence of delirium with a moderate strength of evidence. A low strength of evidence indicated that most do not reduce the risk of 30-day mortality; however the studies were not statistically powered to truly reflect the effects on mortality outcomes.

Comparisons of Systemic Analgesics for Acute Pain

The efficacy and harms associated with various systemic analgesics were evaluated in 3 RCTs involving 214 participants, with sample sizes ranging from 30 to 94.³²⁻³⁴ Acute pain was measured on the 10 cm VAS scale, with a mean baseline of 6.5 cm. There was an unclear risk of bias in all studies, and the evidence was insufficient to permit the estimation of the comparative effects of systemic analgesics for the relief of acute pain. Parenteral analgesics (parecoxib intravenous (IV) vs diclofenac

± meperidine intramuscular (IM), and intrathecal isotonic clonidine vs intrathecal hypertonic clonidine) were compared in 2 studies.^{32,33} Parecoxib IV was favored over diclofenac ± meperidine IM (MD = -0.70; 95 percent CI = -1.04 to -0.36; $P<.0001$); however, this finding was not clinically significant.³²

A statistically significant, although not clinically significant, difference in acute pain relief favoring isotonic clonidine compared with intrathecal hypertonic clonidine post-treatment (MD=-1.69; 95 percent CI = -2.01 to -1.37; $P<.00001$).³³ Another RCT³⁴ comparing the oral analgesics, lysine clonixinate with metamizole, did not find a statistically significant difference in pain relief (MD = -0.43; 95 percent CI = -1.30 to 0.44; $P=.33$). Of note, none of the agents tested in any of these trials are commonly used in clinical practice and indeed, because of its toxic metabolite normeperidine, meperidine should never be used for analgesia in older adults.

Comparisons of Anesthesia for Acute Pain

The comparative efficacy and harms of neuraxial anesthesia, including continuous or single administration spinal or epidural anesthesia, was evaluated in 21 RCTs³⁵⁻⁵⁴ and 1 nRCT.⁵⁵ These trials included a total of 1,062 participants ranging in sample size from 20 to 90. Results from 8 cohort studies⁵⁶⁻⁶³ comparing spinal anesthesia with general anesthesia or other modes of administration of spinal anesthesia was also included in the review, and included a total of 3,086 participants, most of whom were female, and sample sizes ranging from 25 to 1,333. The mean age of participants was between 69.8 and 86.0 years. Acute pain levels were measured on the 10 cm VAS with an average baseline score of 4.7 cm.

In 1 RCT, spinal anesthesia was favored over general anesthesia for the relief of acute pain (MD = -0.86; 95 percent CI = -1.30 to -0.42; $P=.0001$); however, this finding was not considered to be clinically significant. Three RCTs compared standard spinal anesthesia with the addition of clonidine, fentanyl, meperidine, morphine, or sufentanil for post-treatment pain relief. Among patients receiving additional fentanyl or sufentanil, none reported pain following the procedure.^{51,64} In addition, no significant difference in pain relief was found in a study⁴⁵ comparing additional morphine with standard spinal anesthesia (MD = -0.36; 95 percent CI = -1.11 to 0.39; $P=.35$).

Transcutaneous Electrical Neurostimulation (TENS)

TENS includes the application of electrodes with varying amplitudes and frequencies to peripheral nerves in the affected area.⁶⁵ Pooled results from 2 RCTs found significantly greater pain relief for patients receiving TENS therapy compared with sham control (MD = -2.79; 95 percent CI = -4.95 to -0.64; $P=.01$); however, these results were not clinically significant.^{66,67} In 1 trial reporting pain on movement,⁶⁶ significantly greater improvements in pain relief were found for neurostimulation compared with sham control (MD = -3.90; 95 percent CI = -6.22 to -1.58; $P=.001$).

Skin and Skeletal Traction

Once considered an effective treatment modality, skin and skeletal traction are no longer commonly used for the treatment of hip fracture pain. Traditionally, preoperative or skeletal traction was standard care for the hip fracture patient population. The theory was that traction could diminish pain by stabilizing the hip joint and leg, and decrease intracapsular joint pressure.⁹ A

Cochrane systematic review consisting of 10 randomized controlled trials (1,456 participants) noted no benefits for traction.⁶⁸ Skin traction involves bandaging the limb with adhesive tape and attaching a traction sled with weight hung from it.^{69,70} In skeletal traction, pins are inserted into the proximal tibia or distal femur while the patient is under local anesthesia, and weights and ropes are then attached to the pins.⁶⁹ Skin traction, skeletal traction, and no traction were compared in 8 trials^{54,71-77} which found no significant differences among the groups for the reduction of acute pain. However, the strength of evidence for these results was rated as low.

Rehabilitation for Acute Pain

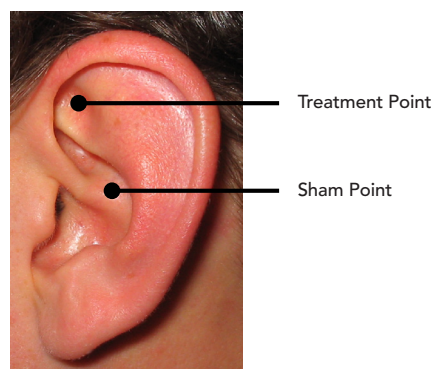
Rehabilitation is a standard approach to postoperative care for patients with hip fractures. Rehabilitation often includes physical therapy and functions to stretch and strengthen the spinal and psoas muscles. Ultimately, the goal of rehabilitation is to increase muscle strength and range of joint motion; however, delirium and pain may limit patient participation.⁹ A statistically significant difference in pain relief was noted in 1 RCT⁷⁸ comparing physical therapy with standard care (MD = -1.39; 95 percent CI = 2.27 to -0.51; $P=.002$); however, these results were not clinically significant.

Complementary and Alternative Medicine (CAM)

Complementary and alternative medicine techniques include auricular acupressure and Jacobsen relaxation. In auricular acupressure, tiny beads are placed on the outer ear at acupuncture points corresponding to the hip.⁷⁹ This is believed to enhance the flow of chi, or life energy, and has a systemic analgesic effect. Acute pain for auricular acupressure was measured on the 10 cm

VAS scale. Jacobsen relaxation, a 2-step process involving the relaxation and contraction of muscles, measured acute pain on the 10-point verbal Sensation of Pain and Distress Scale.⁷⁹

Figure 3. Acupressure vs Sham Control



Source: Kober A, Scheck T, Greher M, et al. *Anesth Analg.* 2002;95(3):723-7.

In 1 RCT,⁸¹ acupressure was found to reduce pain compared with a sham intervention (MD = -3.01; 95 percent CI = -4.53 to 1.49; $P<.0001$). Greater reductions in acute pain were also found for relaxation compared with no relaxation (MD = -1.10; 95 percent CI = -1.43 to -0.77; $P<.00001$); however, this result was not clinically significant.⁸⁰ The overall evidence for CAM interventions was insufficient to make firm conclusions.

Comparative Effects of Pain Interventions on Secondary Outcomes

The review synthesized literature on secondary outcomes including 30-day mortality, delirium associated with pain, length of hospitalization, additional pain medication use, quality of sleep, and health-related quality of life. Patients treated with nerve blocks compared to usual care had a lower risk of cardiovascular mortality; however, these results were nonsignificant. A moderate strength of evidence also favored nerve blocks over usual care for reducing the incidence of delirium.

30-day Mortality

Comparisons of general or spinal anesthesia with epidural anesthesia yielded insufficient evidence to draw firm conclusions regarding the comparative efficacy of these interventions on 30-day mortality outcomes. No significant differences in mortality rates were found in 2 RCTs^{43,82} comparing spinal anesthesia with general anesthesia (10/53 vs 5/46; OR = 1.73; 95 percent CI = 0.53 to 5.68; $P=.36$). In a review of 5 cohort studies,^{56,59,60,62,63} no significant differences in mortality rates were found for spinal anesthesia compared with general anesthesia, although participants receiving continuous spinal anesthesia had lower mortality rates (70/1077 vs 113/1673; OR = 1.08; 95 percent CI = 0.58 to 2.01; $P=.80$). No significant differences in mortality rates were found in the subgroup analysis of single dose spinal anesthesia versus general anesthesia.

1-year Mortality

The literature on 1-year mortality rates and long-term outcomes after hospital discharge are sparse. Two RCTs with 112 participants^{16,17} and 1 retrospective cohort study of 535 participants⁸³ found no significant differences in mortality between nerve blocks and standard care for 1-year mortality.

Delirium

Delirium, a dangerous complication associated with hip fractures, was studied as a secondary outcome of interest. Reported in 1 RCT³⁴ comparing lysine clonixinate with metamizole, the incidence of delirium was not found to be significantly different between the 2 groups OR = 0.96; 95 percent CI = 0.06 to 15.77; $P=.98$). Measured according to the Mini Mental State Examination (MMSE), delirium was reported in 1 RCT³⁹ which compared spinal anesthesia

with general anesthesia. No significant differences were found between the 2 groups, and the evidence was insufficient to make firm conclusions regarding the comparative efficacy of these interventions on delirium incidence.

In a meta-analysis of 4 RCTs,^{20,21,84,85} a significant difference was found favoring nerve blocks over no nerve blocks for the occurrence of delirium (11/242 vs 33/219; OR = 0.33; 95 percent CI = 0.16 to 0.66; $P=.002$). A pooled analysis of 2 cohort studies^{83,86} similarly demonstrated a lower occurrence of delirium for nerve blocks compared with no nerve block (11/227 vs 55/407; OR = 0.24; 95 percent CI = 0.08 to 0.72; $P=.01$). The strength of evidence for these results was rated as moderate.

Additional Pain Medication Use

Pooled results from 7 RCTs^{15,17,26,28,29,84,87} reporting the use of additional pain medications in a total of 378 participants found a significant difference associated with nerve blocks compared with no nerve block (49/197 vs 68/181; OR = 0.32; 95 percent CI = 0.14 to 0.72; $P=.0006$). Similarly, a retrospective cohort study⁸⁶ also reported a statistically significant difference in favor of nerve blocks (0/49 vs 14/50; OR = 0.03; 95 percent CI = 0.00 to 0.44; $P=.01$). In 1 RCT⁸⁰ comparing relaxation with sham control, additional pain medication (meperidine (mg) or morphine (mg)) was needed less in the relaxation group (MD = -8.43; 95 percent CI = -15.11 to -1.75; $P=.01$).

Length of Stay (LOS) for Acute Hospitalization

In 2 RCTs^{43,82} comparing spinal anesthesia with general anesthesia, the LOS was significantly less for the general anesthesia group (MD = 1.69; 95 percent CI = 0.38 to 3.01; $P=.01$). Two retrospective cohort studies reported the LOS for acute hospitalization

associated with nerve blocks.^{23,86,83} Pooled results were not provided due to substantial heterogeneity between the studies; however, both the 3-in-1 nerve block⁸⁶ and the femoral nerve block⁶⁵ showed lower LOS compared to placebo, with an even more favorable result for the 3-in-1 nerve block.

Adverse Events Relating to Pain Medications for Hip Fracture

Overall, the studies were not sufficiently powered to determine differences in adverse effects between treatment groups. Furthermore, few studies reported serious adverse events including myocardial infarction, stroke, and renal failure.

Deep Venous Thrombosis and Pulmonary Embolism

Reported in 2 RCTs^{17,89} including 100 patients, no significant differences with respect to the occurrence of deep venous thrombosis were noted between patients receiving nerve block compared with placebo groups. Another 2 RCTs^{19,84} reporting pulmonary embolism in 128 subjects also found no significant difference between the nerve block group compared with placebo.

Myocardial Infarction and Stroke

Myocardial infarction, a serious adverse event, was reported infrequently throughout the literature. Two RCTs which included 145 total participants^{19,23} reported no significant differences in the occurrence of myocardial infarction among patients receiving nerve block compared with those receiving placebo (1/72 vs 1/73; OR = 1.00; 95 percent CI = 0.06 to 16.67; $P=1.00$). Likewise, another retrospective cohort study⁸³ of 535 subjects comparing nerve blocks to placebo also found no significant differences between the 2 groups.

In 1 RCT⁸⁹ no significant difference in strokes was reported among patients receiving nerve blocks comparing with placebo (2/64 vs. 1/64; OR 1.63; 95 percent CI = 0.19 to 13.61; $P=.65$). Another retrospective cohort study⁸³ of 535 subjects also found no statistically significant difference between these 2 groups.

Hypotension

Larger doses of spinal anesthetic resulted in more hypotension issues without improvements in pain control.⁹⁰ Hypotension was reported in 3 cohort studies of 267 participants.^{57,58,60} A statistically significant reduction in hypotension was associated with 2.5 mg of bupivacaine compared to 5 mg of the medication (15/121 vs 21/161; OR = 0.08; 95 percent CI = 0.03 to 0.23; $P<.00001$). Likewise, a reduction in hypotension was found for 4 mg compared to 12 mg of bupivacaine (3/30 vs 23/30; OR = 0.03; 95 percent CI = 0.01 to 0.15) and for 0.125 percent vs 0.5 percent bupivacaine (4/12 vs 10/13; OR = 0.15; 95 percent CI = 0.03 to 0.87; $P=.03$). In 3 RCTs of 132 subjects^{46,53,91} a significantly lower incidence of hypotension was reported in patients receiving sufentanil compared to no sufentanil (8/66 vs 45/66; OR = 0.05; 95 percent CI = 0.01 to 0.34; $P=.002$).

Respiratory infection

No significant differences were found between groups in 5 RCTs^{17,19,84,89,92} reporting respiratory infection for nerve blocks compared with placebo. However, 1 retrospective cohort study⁸³ found a significant difference between the 2 groups in favor of nerve blocks (9/178 vs 39/357; OR = 0.43; 95 percent CI = 0.21 to 0.92; $P=.03$).

Subpopulation Analyses

Subpopulation characteristics including sex, age, race, marital status, comorbidities, body mass index (BMI), pre-fracture functional status, and family distress were analyzed. The evidence for this key question was lacking or insufficient to draw conclusions regarding the effectiveness and safety of pain management interventions for these prespecified subpopulations.

Patients with pre-existing heart disease were recruited in 1 study¹⁹ which found a significant reduction in acute pain favoring nerve blocks compared with no nerve block (MD = -0.98; 95 percent CI = -1.49 to -0.48; $P < .0001$). No significant differences were found for 30-day mortality, or adverse events including cardiac complications, congestive heart failure, myocardial infarction, respiratory infection, or pulmonary embolism.

Participants who were independent prior to hip fracture were recruited in 1 RCT⁸⁴ which found no significant difference between nerve blocks compared with standard care for 30-day mortality. Another trial⁷⁷ conducted among Asian patients found no difference in acute pain reduction for skin traction compared with placebo.

Limitations of the Review

Despite the extensive research process that was incorporated to gather the existing evidence on pain management interventions for older patients with hip fractures, there were limitations that hindered the ability to draw firm conclusions. Evidence on the comparative effectiveness of pain management interventions was hampered by a lack of standardized evidence-based guidelines for assessing pain specific older patients with a large number of comorbidities. In addition, a stratified analysis of subpopulations within the hip fracture patient

population was rarely found. Broad cognitive assessment tools including the Mini-Mental State Examination were used to differentiate between dementia onset and acute delirium. Although coexisting conditions were frequently present in the hip fracture patient population, risk adjustments used in various studies were not reported. Pre-fracture functional status, an important component which can potentially impact reported pain levels, was rarely reported.

The studies included in this comprehensive review contained small sample sizes and reported a limited number of outcome measures. While several of the studies had poor methodology, there was also a high risk of bias. The strength of evidence was low or insufficient for most outcomes. The effects of long-term pain were not studied. Over half of the studies excluded patients with cognitive impairment, an important subpopulation of interest. The included studies did not exclusively examine patients from institutional settings, which further impaired the external validity or applicability of the findings.

Although the studies included in the review consisted primarily of pharmacologic therapies and mainly focused on the discipline of anesthesiology, additional evidence has shown the benefits of multidisciplinary therapeutic interventions for the attainment of optimal pain management.^{93,94} Other limitations include the narrow scope of regions in which the studies were conducted. Focusing mostly on single centers in Europe and Asia, minimal evidence on the comparative effectiveness of pain interventions was identified in North America. The search was limited to 1990, which leaves little to conclude

about early research and studies for the treatment of pain.

The review presented valid evidence for the reduction of acute pain and delirium with nerve block interventions. However, most of the studies lacked sufficient power to truly detect the differences in adverse effects between treatment groups. In addition, few studies reported serious adverse events including myocardial infarction, stroke, and renal failure. Another limitation was the lack of comparisons for CAM approaches with pharmacological treatments.

The studies identified a reduced need for systemic analgesics. Nonetheless, the clinical significance of this finding is only beneficial if the reduced requirement for systemic analgesics can be associated with a reduction in adverse events. Little evidence exists on the long-term effects of early postoperative pain management, and the management of pain following hospital discharge. Most studies also failed to note whether or not the patients had any negative or positive effects from the intervention which would compromise their ability to mobilize postoperatively.

Directions for Future Research

There is a strong need for larger sample sizes and multicenter studies to address the long-term benefits and adverse events associated with improved pain management. Future studies should also address the effects of pain management interventions on older patients with dementia. Subpopulations of interest should be reviewed in order to determine effects of interventions on factors such as race, gender, age, or other existing comorbidities. The additive benefits of pharmacological interventions with nonpharmacological interventions including rehabilitation

and CAM should be researched. The effects of multimodal pain management should be identified in order to determine if there are additional benefits from the incorporation of a multidisciplinary approach.

More simplified and clinically meaningful conclusions regarding the comparative effectiveness of different pain interventions for patients with hip fractures can be reached through the standardization of outcomes and outcome measures. The multidimensional nature of pain is not reflected in the measured outcomes. Validated pain scores, prescribed opioids and other pharmacologic therapies, adverse effects, and complications attributable to the intervention are all relevant outcomes for future study. Other outcomes including functional pain, quality of life, and recovery time should be researched. Pain assessment scales, which can be used to assess pain in patients that cannot communicate verbally such as patients with delirium or dementia, would also be valuable for future research studies. A significant issue with determining the level of pain for the hip fracture patient is not only the subjective nature of pain, but also the fact that patients may have confusion or dementia inhibiting their ability to convey the degree to which they are suffering. These communication issues can be addressed through other pain assessment tools that use a nonverbal component. In order to effectively determine the efficacy of various interventions for reducing pain intensity, pain assessments should be conducted preoperatively and daily among hospitalized patients. Regular long-term followup is crucial to determine the patient's pain status after discharge from the hospital. Pain outcomes evaluated over the 6 months following the fracture can be used to effectively determine the most appropriate intervention which will

ultimately result in complete recovery for the patient.

Patients with cognitive impairments, including dementia and delirium, are important for future studies as they represent a large fraction of the population affected by hip fractures. Cognitive screening tools could be used to differentiate between acute or chronic delirium in patients with underlying or newly onset dementia. Overall, the standardization of outcome measures and assessment tools to measure pain will minimize bias, which will also provide a more validated approach to determining the most effective strategy to reduce pain in the hip fracture patient.

Conclusions

The sparsity of data available on pain management interventions for hip fractures hinders the ability to make firm conclusions regarding the efficacy of a single approach compared with other approaches for treating hip fracture-related pain. The evidence shows improvements in short-term pain scores for most interventions, but fails to reflect the long-term outcomes, which are important in terms of cost, morbidity, and quality of life. Complication rates were low overall, and adverse events were not significantly different among the interventions studied. High-quality designed trials with a large number of subjects are needed to truly determine the comparative effectiveness of the interventions.

The available evidence from the review identifies the effectiveness of nerve blocks for improved pain relief compared with standard care alone. Furthermore, nerve blocks have the ability to reduce the need for additional systemic analgesia, and may reduce the risk of delirium. Overall, most nerve blocks were able to reduce the intensity of acute pain and the incidence of

delirium. Although most practicing anesthesiologists incorporate nerve blocks in treatment, the time, effort, and supervision required to ensure that they work well has deterred many institutions from using them. A low strength of evidence showed that nerve blocks do not reduce the risk of 30-day mortality; however, the results from studies were not sufficiently powered to fully determine the effects on mortality outcomes.

The review indicated a potential for pain relief with rehabilitation, acupuncture, relaxation therapy, and TENS, but the evidence was insufficient to draw firm conclusions. Spinal anesthesia, used during surgery, did not differ in mortality rates, delirium, or other medical complications of the fracture compared with general anesthesia. Furthermore, the addition of other agents to plain local anesthetic for spinal anesthesia did not make any difference in the outcomes outside of the operating room. Larger doses of spinal anesthesia may induce hypotension, without improvements in pain relief.⁹⁰

Overall, the evidence points to improvements in short-term pain scores for most interventions. The complication rates were generally low and did not differ significantly between interventions. Improvements in the design of trials and larger sample sizes with a greater degree of statistical power will allow for conclusions to be made regarding the comparative effectiveness of various interventions intended to reduce pain following a hip fracture. Until future research is conducted, the management of pain in patients affected by hip fractures is dependent on the available evidence from interventions, staff skills, and an understanding of pre-existing patient comorbidities.

The comprehensive review conducted by the AHRQ on pain management interventions for hip fractures presents the available evidence intended to guide clinicians in making shared and informed decisions for patients suffering from hip fractures. Health care professionals are faced with the challenge of determining how to ultimately treat the pain in an effort to achieve the most optimal outcome. Effective pain management has the potential to reduce the risk for pulmonary embolism and deep venous thrombosis, in addition to reducing the incidence of delirium and the length of hospitalization. A challenge for health care providers is determining the patient's pain levels. With many affected individuals already experiencing dementia and cognitive impairment, the ability to adequately assess the pain can be difficult. Validated measures and scales are necessary. Several studies found statistically significant differences in pain reported according to the *P*-value, but these findings were not clinically significant. Studies in various populations have shown that a meaningful change in pain scores corresponds to at least a 0.9 to 1.3 cm reduction on the 10 cm VAS. In other words, a statistically significant reduction in acute pain may not be deemed clinically significant enough to allow for improvements in the patient's self-reported pain level and functional status.

Current research generally suggests that effective pain management will improve outcomes for older patients who are hospitalized after hip fractures. The evidence indicates that well-managed pain will allow patients more comfort and mobility, shorter length of hospitalizations, reduced delirium, and an enhanced quality of life. The AHRQ systematic review indicates that most nerve blocks, especially femoral and fascia iliaca blocks, are effective for significantly reducing pain intensity in these patients. However, research on the comparative benefits and risks of pain management interventions for hip fracture patients is still in its infancy. In addition to the overall question of which interventions are most effective, clinicians need to know:

- Whether nerve blocks are more efficacious and associated with fewer side effects and better outcomes than standard opioid therapies
- Whether certain subpopulations will benefit more from nerve blocks or standard opioid therapy
- Whether there are differences between opioid agents in terms of efficacy, side effect profiles, and other outcomes
- What roles nonpharmacologic approaches might play in combination treatments

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